Appl. No. 10/663,215 Amdt. dated December 15, 2003 Reply to Notice to File Missing Parts of December 9, 2003

## Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

## **Listing of Claims:**

Claim 1 (original): A use of an isolated peptide of 40 or fewer amino acids, comprising a sequence with at least 90% identity to a sequence  $TFSX_1LIX_2IFQ$  (SEQ ID NO:4), where  $X_1$  and  $X_2$  are independently selected from amino acids with a charge under physiological conditions, and wherein said peptide, when presented as an antigen, raises antibodies which bind to and cause destruction of pathologically adherent erythrocytes, for the manufacture of a medicament to cause destruction of erythrocytes that adhere to vascular endothelial cells due to a pathological condition.

Claim 2 (original): A use of claim 1, wherein  $X_1$  and  $X_2$  are both negatively charged.

Claim 3 (original): A use of claim 1, wherein  $X_1$  and  $X_2$  are both positively charged.

Claim 4 (original): A use of claim 1, wherein  $X_1$  and  $X_2$  are both lysine.

Claim 5 (original): A use of claim 1, wherein one or more of said amino acids is a D- amino acid.

Claim 6 (original): A use of claim 1, wherein said peptide has the sequence TFSKLIKIFQ (SEQ ID NO:3).

Claim 7 (original): A use of claim 1, wherein said pathological condition is selected from the group consisting of diabetes, thalassemia, sickle cell anemia, and malaria.

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Claim 8 (original): A use of claim 1, wherein said medicament comprises antibodies.

Claim 9 (original): A use of claim 8, wherein said antibodies are polyclonal.

Claim 10 (original): A use of claim 8, wherein said antibodies are monoclonal.

Claim 11 (original): A use of claim 10, wherein said monoclonal antibodies are humanized.

Claim 12 (original): A use of a nucleic acid encoding an isolated peptide of 40 or fewer amino acids, comprising a sequence at least 90% identical to a sequence TFSX<sub>1</sub>LIX<sub>2</sub>IFQ (SEQ ID NO:4), where X<sub>1</sub> and X<sub>2</sub> are independently selected from amino acids with a charge under physiological conditions, and wherein antibodies raised by said peptide bind to and cause destruction of pathologically adherent erythrocytes, for the manufacture of a medicament to cause destruction of erythrocytes that adhere to vascular endothelial cells due to a pathological condition.

Claim 13 (original): A use of claim 12, wherein  $X_1$  and  $X_2$  are both negatively charged.

Claim 14 (original): A use of claim 12, wherein  $X_1$  and  $X_2$  are both positively charged.

Claim 15 (original): A use of claim 12, wherein  $X_1$  and  $X_2$  are both lysine.

Claim 16 (original): A use of claim 12, wherein said pathological condition is selected from the group consisting of diabetes, thalassemia, sickle cell anemia, and malaria.

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Claim 17 (original): A method for lysing erythrocytes adherent due to a pathological condition, said method comprising administering to a patient with said adherent erythrocytes antibodies that specifically bind to a protein having an amino acid sequence YETFSKLIKIFQDH (SEQ ID NO:5) on said erythrocytes, wherein binding of said antibodies to said amino acid sequence results in destruction of said adherent erythrocytes.

Claim 18 (original): A method of claim 17, wherein said pathological condition is selected from the group consisting of diabetes, thalassemia, sickle cell anemia, and malaria.

Claim 19 (original): A method for lysing erythrocytes adherent due to a pathological condition, said method comprising administering to a patient with said pathologically adherent erythrocytes an isolated peptide with at least 80% sequence identity to a sequence YX<sub>1</sub>TFSX<sub>2</sub>LIX<sub>3</sub>IFQX<sub>4</sub>X<sub>5</sub> (SEQ ID NO:6), or a fragment thereof, which peptide or fragment thereof, when presented as an antigen, raises antibodies which specifically bind to and cause destruction of said pathologically adherent erythrocytes, wherein X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub>, X<sub>4</sub> and X<sub>5</sub> are independently selected from amino acids that bear a charge at physiological pH.

Claim 20 (original): A method of claim 19, wherein  $X_1$  and  $X_4$  bear the same charge and  $X_2$  and  $X_3$  bear the same charge, but the charge borne by  $X_1$  and  $X_4$  is not the same as the charge borne by  $X_2$  and  $X_3$ .

Claim 21 (original): A method of claim 20, wherein the charge borne by  $X_2$  and  $X_3$  is positive.

Claim 22 (original): A method of claim 19, wherein  $X_2$  and  $X_3$  are lysine residues.

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Claim 23 (currently amended): A method of claim 19, wherein said peptide has 100% sequence identity to SEQ ID:6 SEQ ID NO:6 and further wherein  $X_2$  and  $X_3$  are lysine residues,  $X_1$  is a glutamic acid,  $X_4$  is an aspartic acid and  $X_5$  is a histidine (SEQ ID NO:5).

Claim 24 (original): A method of claim 19, wherein one or more of said amino acids is a D- amino acid.

Claim 25 (original): A method for lysing erythrocytes adherent due to a pathological condition, said method comprising administering to a patient with said pathologically adherent erythrocytes a nucleic acid encoding a peptide with at least 80% sequence identity to the sequence YX<sub>1</sub>TFSX<sub>2</sub>LIX<sub>3</sub>IFQX<sub>4</sub>X<sub>5</sub> (SEQ ID NO:6), or fragment thereof which raises antibodies which specifically recognize said peptide, wherein X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub>, X<sub>4</sub>, and X<sub>5</sub> are independently selected from amino acids that bear a charge at physiological pH, wherein expression of said peptide raises antibodies which specifically bind to and cause destruction of said pathologically adherent erythrocytes.

Claim 26 (original): A method of claim 25, wherein  $X_1$  and  $X_4$  bear the same charge and  $X_2$  and  $X_3$  bear the same charge, but the charge borne by  $X_1$  and  $X_4$  is not the same as the charge borne by  $X_2$  and  $X_3$ .

Claim 27 (original): A method of claim 25, wherein the charge borne by  $X_2$  and  $X_3$  is positive.

Claim 28 (original): A method of claim 25, wherein  $X_2$  and  $X_3$  are lysine residues.

Claim 29 (currently amended): A method of claim 25, wherein said peptide has 100% sequence identity to  $\frac{\text{SEQ ID}.6}{\text{SEQ ID NO}.6}$  and further wherein  $X_2$  and  $X_3$  are lysine residues,  $X_1$  is a glutamic acid,  $X_4$  is an aspartic acid and  $X_5$  is a histidine (SEQ ID NO:5).

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Claim 30 (original): A composition of an isolated peptide of the formula with at least 80% sequence identity to a sequence  $YX_1TFSX_2LIX_3IFQX_4X_5$  (SEQ ID NO:6), wherein  $X_1$ ,  $X_2$ ,  $X_3$ ,  $X_4$  and  $X_5$  are independently selected from amino acids that bear a charge at physiological pH, and wherein antibodies raised by said peptide bind to and cause destruction of pathologically adherent erythrocytes, and a pharmaceutically acceptable carrier.

Claim 31 (original): A composition of claim 30, wherein  $X_1$  and  $X_4$  bear the same charge and  $X_2$  and  $X_3$  bear the same charge, but the charge borne by  $X_1$  and  $X_4$  is not the same as the charge borne by  $X_2$  and  $X_3$ .

Claim 32 (original): A composition of claim 30, wherein the charge borne by  $X_2$  and  $X_3$  is positive.

Claim 33 (original): A composition of claim 30, wherein  $X_2$  and  $X_3$  are lysine residues.

Claim 34 (original): A composition of claim 30, wherein said peptide has 100% sequence identity to SEQ ID NO:6 and further wherein  $X_2$  and  $X_3$  are lysine residues,  $X_1$  is a glutamic acid,  $X_4$  is an aspartic acid, and  $X_5$  is a histidine (SEQ ID NO:5).

Claim 35 (original): A composition of claim 30, wherein one or more of said amino acids is a D- amino acid.

Claim 36 (original): An isolated peptide with at least 80% sequence identity to the sequence  $YX_1TFSX_2LIX_3IFQX_4X_5$  (SEQ ID NO:6) or fragment thereof, which peptide or fragment, when presented as an antigen, raises antibodies that specifically bind to SEQ ID NO:5 and cause destruction of pathologically adherent erythrocytes and wherein  $X_1$ ,  $X_2$ ,  $X_3$ ,  $X_4$  and  $X_5$  are independently selected from amino acids that bear a charge at physiological pH.

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Claim 37 (original): An isolated peptide of claim 36, wherein  $X_1$  and  $X_4$  bear the same charge and  $X_2$  and  $X_3$  bear the same charge, but the charge borne by  $X_1$  and  $X_4$  is not the same as the charge borne by  $X_2$  and  $X_3$ .

Claim 38 (original): An isolated peptide of claim 36, wherein the charge borne by  $X_2$  and  $X_3$  is positive.

Claim 39 (original): An isolated peptide of claim 36, wherein  $X_2$  and  $X_3$  are lysine residues.

Claim 40 (original): An isolated peptide of claim 36, which peptide has 100% sequence identity to SEQ ID NO:6 and further wherein  $X_2$  and  $X_3$  are lysine residues,  $X_1$  is a glutamic acid,  $X_4$  is an aspartic acid and  $X_5$  is a histidine (SEQ ID NO:5).

Claim 41 (original): An isolated peptide of claim 36, wherein one or more of said amino acids is a D- amino acid.

Claim 42 (original): An isolated nucleic acid encoding a peptide with at least 80% sequence identity to  $YX_1TFSX_2LIX_3IFQX_4X_5$  (SEQ ID NO:6) or a fragment thereof, which peptide or fragment, when presented as an antigen, raises antibodies that specifically bind to SEQ ID NO:5 and cause destruction of pathologically adherent erythrocytes and further wherein  $X_1$ ,  $X_2$ ,  $X_3$ ,  $X_4$ , and  $X_5$  are independently selected from amino acids that bear a charge at physiological pH.

Claim 43 (original): An isolated nucleic acid of claim 42, wherein  $X_1$  and  $X_4$  bear the same charge and  $X_2$  and  $X_3$  bear the same charge, but the charge borne by  $X_1$  and  $X_4$  is not the same as the charge borne by  $X_2$  and  $X_3$ .

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Claim 44 (original): An isolated nucleic acid of claim 42, wherein the charge borne by  $X_2$  and  $X_3$  is positive.

Claim 45 (original): An isolated nucleic acid of claim 42, wherein  $X_2$  and  $X_3$  are lysine residues.

Claim 46 (original): An isolated nucleic acid of claim 42, wherein said encoded peptide has 100% sequence identity to SEQ ID NO:6 and further wherein  $X_2$  and  $X_3$  are lysine residues,  $X_1$  is a glutamic acid,  $X_4$  is an aspartic acid, and  $X_5$  is a histidine (SEQ ID NO:5).

Claim 47 (original): An isolated nucleic acid of claim 42 operably linked to a promoter.

Claim 48 (original): An isolated nucleic acid of claim 46 operably linked to a promoter.

Claim 49 (original): A composition of an isolated nucleic acid encoding a peptide with at least 80% sequence identity to the sequence  $YX_1TFSX_2LIX_3IFQX_4X_5$  (SEQ ID NO:6) or fragment thereof, which peptide or fragment, when presented as an antigen, raises antibodies that specifically bind to SEQ ID NO:5 and cause destruction of pathologically adherent erythrocytes, wherein  $X_1$ ,  $X_2$ ,  $X_3$ ,  $X_4$ , and  $X_5$  are independently selected from amino acids that bear a charge at physiological pH, and a pharmaceutically acceptable carrier.

Claim 50 (original): A composition of claim 49, wherein  $X_2$  and  $X_3$  are lysine residues,  $X_1$  is a glutamic acid,  $X_4$  is an aspartic acid, and  $X_5$  is a histidine (SEQ ID NO:5).